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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/713,472	11/14/2003	Charles A. Vacanti	07917-082003	1928
23579	7590	05/18/2005	EXAMINER	
PATREA L. PABST PABST PATENT GROUP LLP 400 COLONY SQUARE SUITE 1200 ATLANTA, GA 30361			GAMETT, DANIEL C	
			ART UNIT	PAPER NUMBER
			1647	

DATE MAILED: 05/18/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/713,472

Applicant(s)

VACANTI ET AL.

Examiner

Daniel C. Gamett

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 April 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 43,44 and 54 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 43,44 and 54 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 14 November 2003 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 12/10/2004.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Status of the Application, Amendments, and Claims

1. The Examiner for this Application is now Daniel C. Gamett, Art Unit 1647.
2. Applicant's election without traverse of claims 43 and 44 in the reply filed on 04/04/2005 is acknowledged.
3. The amendment of 04/04/2005 has been entered in full. Claims 22-42 are cancelled. New claim 45 has been added. Claims 43-45 are under examination.

Objections

4. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claim 45 been renumbered 54.

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Neuroendocrine stem cells from adult mammalian adrenal gland or pancreas.

6. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference signs) not mentioned in the description. "10, 12, 14, 16, and 18".

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A proposed drawing correction, corrected drawings, or amendment to the specification to add the reference sign(s) in the description, are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Priority

7. The Examiner has concluded that the earliest application in the chain of priority to this application, serial number 09/066,038, PAT 6027744, filed 04/24/1998, is not enabling for an isolated neuroendocrine stem cell, which is the subject matter of the pending claims this application. Accordingly, the subject matter defined in claims 43, 44, and 54 has an effective filing date of 11/25/1998, which is the earliest date on which this exact specification was filed.

8. Should the applicant disagree with the examiner's factual determination above, it is incumbent upon the applicant to provide the serial number and specific page numbers of any parent application filed prior to 11/25/1998 which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession of and fully enabled for prior to 11/25/1998.

35 U.S.C. § 112, Second Paragraph

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claim 54 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 54 is drawn to a stem cell of claim 43, wherein the cell is isolated by

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digestion of the tissue with trypsin and isolation of the cells by centrifugation at 1200 rpm for five minutes. The method step of centrifugation at 1200 rpm is unclear because the actual conditions of centrifugation could vary greatly depending on the radius of the centrifuge rotor.

35 U.S.C. § 112, First Paragraph

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 43, 44, and 54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 43 is drawn to an isolated, mammalian adult neuroendocrine stem cell. Claims 44 and 54 are drawn to a stem cell of claim 43, wherein the cell is isolated from adrenal gland or pancreas tissue (claim 44) and wherein the cell is isolated by digestion of the tissue with trypsin and isolation of the cells by centrifugation at 1200 rpm for five minutes (claim 54). The specification does indeed describe a procedure in which cells are derived from adrenal and pancreatic tissues (example 9). The cells thus produced are asserted to be “neuroendocrine stem cells” but the only characterization given is that they are “small, round” (p. 52, lines 12-14). The specification describes neuroendocrine stem cells as being “found in areas such as the adrenal medulla and differentiate into cells that make catecholamines such as epinephrine and norepinephrine, and also from the pancreas, in which case they develop into cells that secrete

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insulin (beta cells) or glucagon (alpha cells)” (p. 26, lines 15-20). Furthermore, the art-accepted usage of the term “stem cell” carries the implication that the cell has a capacity for extended proliferation and self-renewal (see Weiss et al., US Patent 5750376, col. 2, line 61 to col. 3, line 4; listed on IDS filed 12/10/2004). At the time of the invention (1998), the existence of stem cells in the pancreas was only beginning to be recognized in the art. In 1996, Bouwens and Blay (J. Histochemistry and Cytochemistry 44(9):947-151; 1996; listed on IDS filed 12/10/2004) were unable to find cells expressing known stem cell markers in the pancreas of postnatal rats. Evidence for pluripotent stem cells from adult pancreas was published in 1997 (Cornelius *et al.*, Horm. Metab. Res. 1997 Jun;29(6):271-277; listed on IDS filed 12/10/2004) but the characterization of such cells was still ongoing in 2001 (Zulewski *et al.*, Diabetes. 2001 Mar;50(3):521-33; listed on IDS filed 12/10/2004). Adrenal medullary chromafin cells can assume neuronal properties in certain conditions (Notter et al., Cell Tissue Res. 244: 69-76 (1986); listed on IDS filed 12/10/2004) but this is considered to be a case of transdifferentiation, not stem cell activity as described in the instant specification. The Examiner could find no publication suggesting the presence of stem cells in the adult adrenal medulla, although the existence of a stem cell zone in the adult rat adrenal cortex has been proposed several years after the filing of the instant specification (Mitani *et al.*, Biochim Biophys Acta. 2003 Feb 17;1619(3):317-24). Given the state of the art, a claim to a neuroendocrine stem cell isolated from pancreas or adrenal gland should be accompanied by characterization of the capacity of the isolated cells for proliferation, self-renewal, and differentiation. The person of skill in the art at the time of the invention would not recognize “small” and “round” as being definitive

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characteristics of neuroendocrine stem cells isolated from either the pancreas or the adrenal gland.

13. Claims 43, 44, and 54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 43 is drawn to an isolated, mammalian adult neuroendocrine stem cell. Claims 44 and 54 are drawn to a stem cell of claim 43, wherein the cell is isolated from adrenal gland or pancreas tissue (claim 44) and wherein the cell is isolated by digestion of the tissue with trypsin and isolation of the cells by centrifugation at 1200 rpm for five minutes (claim 54). As discussed above, it is not clear that the cells isolated in example 9 comprise neuroendocrine stem cells. Therefore, the specification does not teach how to make the claimed invention. The procedure described in example 9 would be expected to yield a mixed population of cells of which only a fraction, if any, are neuroendocrine stem cells. The specification directs the skilled artisan toward small, round cells, of which there are “many” (p. 52, lines 12-14), and describes some characteristics of cells that can be derived from the stem cells (p. 26, lines 15-20), but leaves it to the artisan to do the experimentation necessary to provide “an isolated, mammalian adult neuroendocrine stem cell.” Due to the large quantity of experimentation necessary to determine if a population of cells comprises stem cells, the lack of direction/guidance presented in the specification regarding the capacity of the isolated cells for proliferation, self-renewal, and differentiation, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which established the unpredictability of finding stem cells in adult mammalian pancreas or adrenal gland, and the

breadth of the claims which fail to recite functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

35 U.S.C. § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 43 and 44 are rejected under 35 U.S.C. 102(b) as being anticipated by Cornelius *et al.*, Horm. Metab. Res. 1997 Jun; 29(6):271-277 (listed on IDS filed 12/10/2004). Claim 43 is drawn to an isolated, mammalian adult neuroendocrine stem cell. Claim 44 is drawn to a stem cell of claim 43, wherein the cell is isolated from adrenal gland or pancreas tissue. Cornelius *et al.*, teach (whole document) the isolation and characterization of pluripotent stem cells from the pancreas of adult mice. These cells were shown to be capable of long-term culture and to differentiate into cells that express insulin, glucagon, and somatostatin.

Conclusion

16. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel C Gamett, Ph.D., whose telephone number is 571 272 1853. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571 272 0961. The fax phone number for the organization where this application or proceeding is assigned is 571 273 8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DCG
Art Unit 1647
11 May 2005

Elizabeth C. Kemmerer

**ELIZABETH KEMMERER
PRIMARY EXAMINER**